Award Number: W81XWH-11-1-0823

TITLE: Preclinical Evaluation of a Decision Support Medical Monitoring System for Early Detection of Potential Hemodynamic Decompensation During Blood Loss in Humans

PRINCIPAL INVESTIGATOR: Michael J. Joyner, M.D.

CONTRACTING ORGANIZATION: Mayo Clinic,
Rochester, MN

REPORT DATE: September 2013

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	**2. REPORT TYPE**	**3. DATES COVERED**
September 2013	Final	15 September 2011 - 14 August 2013

4. TITLE AND SUBTITLE

Preclinical Evaluation of a Decision Support Medical Monitoring System for Early Detection of Potential Hemodynamic Decompensation During Blood Loss in Humans

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-11-1-0823

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
MIchael J. Joyner, M.D.

E-Mail: joyner.michael@mayo.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Mayo Clinic
200 First Street SW
Rochester, MN 55905

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Please see next page.

15. SUBJECT TERMS
Blood loss; decision support; resuscitation

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
U	U	U	UU	7	**19b. TELEPHONE NUMBER** *(include area code)*

14. ABSTRACT

The goal of this research is to perform a preclinical evaluation of a non-invasive medical monitoring device to predict blood loss and hemorrhage in humans. The aim is to be able to detect subtle changes in hemodynamic variables that provide prodromal clues to impending cardiovascular collapse. This will enhance the ability of first responders (medics), nurses, and physicians to intervene with appropriate resuscitative steps in individuals who have suffered injuries during combat. Since the last progress report we have studied a total of 12 subjects. These individuals have been subjected to -15, -30, and -45 mmHg of lower body negative pressure (LBNP) and sequential blood loss of 333, 666, and 1 L total. Three abstracts related to this work have been presented and two additional abstracts have been submitted for presentation, the high-resolution physiological records have been obtained for subsequent processing by machine learning algorithms, and further off-line validation of the cardiovascular reserve index (CRI) approach develop at the US Army Institute of Surgical Research Labs. In general, our preliminary data shows that there is good agreement for a number of physiological (blood pressures, CVP etc.) variables when LBNP is compared to blood loss and also good agreement between human and prior animal data. Nuances of the data are still being analyzed in collaboration with our colleagues at the U.S. Army Institute of Surgical Research

Table of Contents

Introduction

This report details results from the last year of study entitled “Preclinical Evaluation of a Decision Support Medical Monitoring System for Early Detection of Potential Hemodynamic Decompensation During Blood Loss in Humans.” This technology was developed based on a simulated hemorrhage model using LBNP. Over the last year we have compared results obtained using LBNP with real 1-L blood loss. A total of 12 studies have been completed. In randomized order, six studies were performed with LBNP followed by 1 L of blood loss and six studies were conducted with 1 L of blood loss followed by the LBNP protocol. Approximately 1 hour of rest was given between protocols and all the blood was re-infused immediately following the blood loss protocol.

Body

As noted above, we have completed 12 studies comparing 1 L of blood loss to LBNP up to -45 mmHg. The subjects were instrumented to measure arterial pressure (brachial artery catheter) and central venous pressure via a PICC line. Additional non-invasive monitors including ECG, pulse oximetry, non-invasive finger blood pressure, and other non-invasive monitors were also used. The LBNP protocol consisted of -15, -30, and -45 mmHg for 5 min each. The blood loss protocol consisted of 333 mL of blood removed at each of three stages for a total of 1 L of blood loss. Half the subjects completed LBNP first; the other half completed blood loss first. Blood was also drawn at selected time points to measure various markers of coagulation and also other hormonal measurements.

Key research accomplishments

To date we have completed the initial 12 studies. We have published 3 abstracts, submitted 2 additional abstracts, are currently conducting detailed analysis of the data with our collaborators in San Antonio, and beginning the generation of the relevant manuscripts.

Additionally, we have identified key subject matter and hypotheses for follow-up studies that will begin in the fall of 2013.

Reportable Outcomes

Figures 1 and 2 show the respective CVP and heart rate, changes associated with LBNP and blood loss in our subjects. Although there are some differences in hemodynamics between LBNP and blood loss at corresponding stages (e.g. Figures 1 and 2), nearly all hemodynamic variables that we monitored appear to fall on similar trajectories throughout the attained ranges of CVP, regardless of protocol. Figure 3 is an example of how the heart rate responses fall on similar trajectories in each protocol throughout the attained CVP.

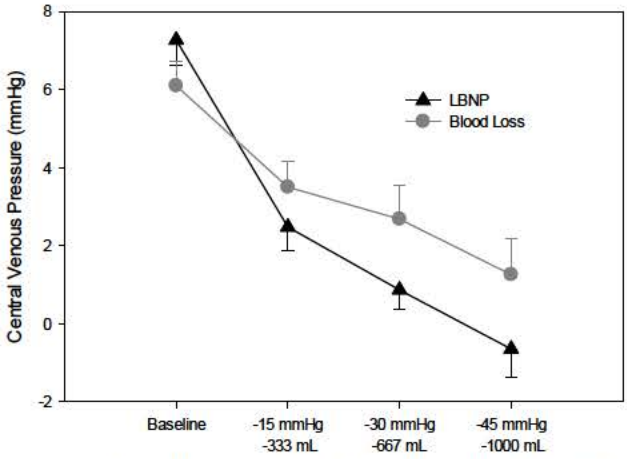

Figure 1. CVP is lower during LBNP vs. Blood Loss at each stage.

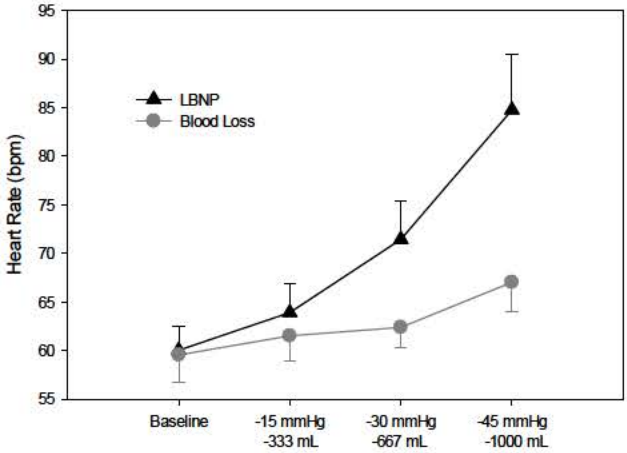

Figure 2. HR is higher during LBNP vs. Blood Loss during the last two stages.

Conclusion

The last year has been highly successful and we have completed the main aims of the initial funding cycle. In general, the hemodynamic responses to LBNP and real blood loss were quite similar. There were

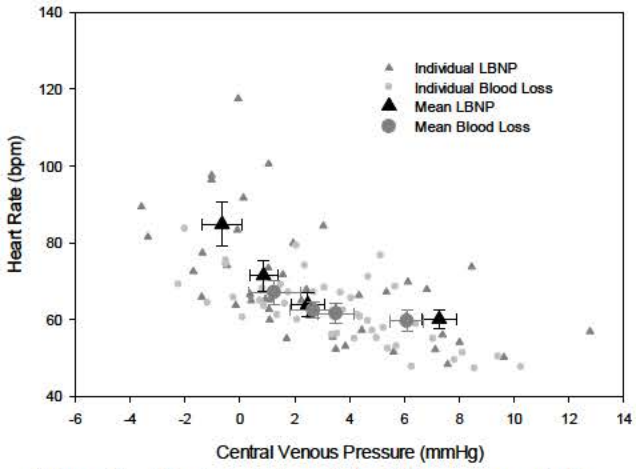

Figure 3. The trajectories of the HR responses during each protocol are similar across the range of CVP.

some subtle differences seen in the heart rate responses at higher levels of LBNP. These nuances are being further evaluated to determine if there was an order effect (LBNP versus blood loss first or second), however much of this effect is likely due to the bigger changes in CVP evoked by LBNP than blood loss. Additionally, we are collaborating with colleagues in San Antonio to evaluate the CRI algorithm and compare blood loss versus LBNP. Importantly, peer-reviewed manuscripts are in the process of being generated and additional follow-up studies are in the process of being conducted.

References

N/A

Appendices

N/A